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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,797	11/20/2001	Joseph S. Adorante	2732	1582

26822 7590 02/23/2004

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EXAMINER

MURPHY, JOSEPH F

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/989,797

Applicant(s)

ADORANTE ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10292002 11202001</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Formal Matters

Claims 1-5 are pending and under consideration.

Information Disclosure Statement

References 8, 10-16, 18 on the information disclosure statement filed 11/20/2001 fail to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The citation should include the author and publication date. It has been placed in the application file, but the information referred to therein has not been considered. Applicant is advised that the date of any re-submission of an item of information contained in an information disclosure statement or the submission of any missing element(s) is the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements. See MPEP § 609 C(1-2).

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase wherein “the channel blocker demonstrating both a transient and a persistent current”. It is not clear how the channel blocker could have a current.

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Presumably, the claim is meant to recite that the cell comprising the ion channels would exhibit the currents, however, as written, the claim is indefinite. Claims 2-4 are rejected insofar as they depend on this recitation in claim 1.

Claim 3 is vague and indefinite in the recitation of the term "very similar". The term "very similar" is a relative term which renders the claim indefinite. The term "very similar" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claim 5 is vague and indefinite in the recitation of the term "screen". It is not clear whether the use of this term is meant to denote that the claim covers an apparatus for carrying out a method, or whether the claim is directed to a method of identifying a Na⁺ channel blocker. The specification does not define the term screen, and thus one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

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evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/41166 (Tsien et al.) in view of US 5,981,268 (Kovacs et al.) and further in view of Gleitz et al. (1995).

The claims are drawn to a method of identifying a Na⁺ channel blocker using a voltage sensitive dye, stimulating an action potential with an external stimulus electrode, and monitoring the membrane potential using optical means, and differentiating the activity of the voltage gated Na⁺ channel for the Na⁺ pump using ouabain. This method is not patentable over the references for the following reasons.

Tsien et al. teaches methods of assaying for small changes in transmembrane potential using voltage sensitive dyes and optically measuring the change in membrane potential (page 3, lines 1-25). Tsien et al. teach methods of screening for potential therapeutic drugs that affect membrane potentials in living cells (page 42). Tsien et al. further teach the use of cells which have been transfected with nucleic acids encoding, inter alia, ion channels (page 44, lines 1-5). Tsien et al. further teaches the use of cell lines including HEK293, LM(TK-), COS, and CHO cells (page 44, lines 7-11). It is an expected property of these cells that they have a potassium conductance which will be altered by varying the potassium concentration, and it is also an expected property of these cells to comprise the Na/K ATPase. Tsien et al. teaches that the transfected cells are treated with a stimulus that modulates the ion channel (page 43, lines 15-20). Tsien et al. teaches that the ion channel may be a sodium, potassium, or calcium channel,

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which may be voltage-gated (page 43, lines 27-31). While Tsien et al. does not teach a method wherein a stimulating current is used to generate an action potential, or the use of tetrodotoxin (TTX), the '268 patent discloses a method of using hybrid biosensors to measure the effect of compounds on the impedance, action potential parameters and membrane conductance of cells comprising voltage gated Na⁺ channels (column 2 lines 39-67). The '268 patent discloses methods wherein the effects of specific ion channel blockage on single electrode impedances were monitored over time as the highly specific blocker of voltage gated Na⁺ channels (TTX) was added (column 18, lines 14-21). The '268 patent further discloses methods wherein a stimulating current is passed to initiate an action potential (column 19, lines 40-44). Neither Tsien nor the '268 patent teaches the method wherein the cell is pretreated with ouabain, however, Gleitz et al. (Gleitz J, Beile A, Peters T. (+/-)-Kavain inhibits veratridine-activated voltage-dependent Na⁽⁺⁾-channels in synaptosomes prepared from rat cerebral cortex. *Neuropharmacology*. 1995 Sep;34(9):1133-8) teaches a method of measuring the effect of kavain on veratridine-induced Na⁺ influx in synaptosomes prepared from rat cerebral cortex (Gleitz at 1134, column 1, first paragraph). In this method the synaptosomes were pretreated with ouabain to inhibit the sodium pump and increase the internal sodium concentration in the presence of kavain, thus showing the effectiveness of using ouabain to differentiate the effect of the sodium pump on Na⁺ concentration (and thus membrane potential) as opposed to the effect on membrane potential of voltage gated Na⁺ channels.

Thus it would have been obvious to one of skill in the art at the time the invention was made to practice a method of identifying a Na⁺ channel blocker using a voltage sensitive dye, stimulating an action potential with an external stimulus electrode, and monitoring the membrane

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potential using optical means, and differentiating the activity of the voltage gated Na⁺ channel for the Na⁺ pump using ouabain. The motivation is provided in the Tsien et al. reference that teaches that the method using voltage sensitive dyes is sensitive to small changes in transmembrane potentials, and can respond on a rapid, millisecond timescale to changes in membrane potentials (page 2, lines 30-38) and in the '268 patent which discloses that biosensors can utilize the highly sensitive nature of biological materials to detect directly the presence or absence of analytes by their affect upon cellular metabolism and that utilizing cultured cell systems it is possible to screen for a broad range of toxins, achieving a fast response time, while maintaining high sensitivity.

Conclusion

No claim is allowed.

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Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

A handwritten signature in black ink, appearing to be 'J. F. Murphy', with a long horizontal flourish extending to the right.

Joseph F. Murphy, Ph. D.
Patent Examiner
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February 11, 2004